

Letters to the Editor

White Cell Count,
Mortality, and Metabolic
Syndrome in the Baltimore
Longitudinal Study of Aging

Ruggiero et al. (1) have shown that higher white cell counts (WCCs) are associated with higher mortality from both cardiovascular disease and cancer. There also was a positive correlation of the WCC with body mass index and triglyceride levels and a negative correlation with physical activity. Waist circumference, waist-to-hip ratio, or high-density lipoprotein levels were not recorded in this study. We believe that if the criteria to diagnose the metabolic syndrome were available they would have explained the elevated WCC, and that the presence of the metabolic syndrome likely would have been the causal factor for both the elevated WCC and the increased mortality.

The metabolic syndrome is an inflammatory state associated with an elevated WCC caused by leucocyte infiltration of an increased mass of intraperitoneal fat. Pickup et al. (2) in 1998 provided evidence that type 2 diabetes was associated with increased concentrations of markers of the acute-phase response, including sialic acid, alpha-1 acid glycoprotein, amyloid A, C-reactive protein, and cortisol. The major cytokine involved in this inflammatory state is interleukin-6, which stimulates hepatic production of C-reactive protein (3). Recently, Tsai et al. (4) have shown that after adjustment for age, gender, and other known risk factors, the greater the number of features of the metabolic syndrome that are present, the higher were the total leukocyte, monocyte, neutrophil, and lymphocyte counts and the higher was the risk of ischemic cardiovascular disease in patients with type 2 diabetes. Similarly, Shim et al. (5) have shown that the greater the number of components of the metabolic syndrome, the more elevated was the WCC.

Although obesity, without features of the metabolic syndrome, has been shown to be associated with an increased WCC, Desai et al. (6) showed that the association of the leukocyte count with obesity is highly dependent on the presence of the metabolic syndrome. In the National Health and Nutrition Examination Survey, an elevated WCC was independently associated with insulin resistance (7).

Therefore, we believe that the association between an elevated WCC and mortality simply reflects the co-association between the metabolic syndrome and mortality. Had assessments of waist-to-hip ratio and the triglyceride-to-high-density lipoprotein ratio been available, we believe that this relationship would have been apparent.

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Reply

We thank Drs. Bell and O'Keefe for the interest in our study about the relationship between the white blood cell (WBC) count and mortality over the period 1958 to 2002 (1).

Drs. Bell and O'Keefe point out that the metabolic syndrome (MetS) could mediate the relationship between elevated WBC count and increased mortality shown in our study. Although we find this hypothesis interesting, we do not have adequate data to address it in the BLSA (Baltimore Longitudinal Study of Aging). Information on the components of the MetS were not systematically collected over the period 1958 to 2002, and therefore we could not explore possible secular trends for this syndrome. Although the mortality risk ratio between WBC groups was adjusted for some components of MetS, such as triglycerides, blood pressure, and diabetes status, we could not investigate the role of waist circumference, waist-to-hip ratio, or high-density lipoprotein levels. Data on waist circumference were available for a small subgroup of the BLSA study population, and high-density lipoprotein was measured starting in the mid-1980s. Other longitudinal studies exist that collected information on the MetS and may better discern whether the presence of MetS is causal in both the elevated WBC count and the increased mortality.

The finding that WBC count is nonlinearly associated with all-cause mortality and almost linearly associated with cardiovascular mortality, while there is no significant association between WBC count and cancer mortality, supports hypotheses that elevated WBC count may be part of a cluster of risk factors that predispose an individual to cardiovascular morbidity and mortality (2). However, whether this cluster corresponds to the MetS is still uncertain.